

steroid hormone receptor gene, a drug resistance gene, an immunomodulation gene, a cell proliferation gene and an apoptosis gene, or a complementary nucleic acid thereto.

38. (Amended) A method for identifying an anticancer therapy, comprising:

(a) detecting, before and after administering a candidate anticancer therapy to a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell,

(i) in a plurality of cells obtained from a body fluid of the subject, an absence or presence of at least one nucleic acid selected from the group consisting of a first cancer-specific nucleic acid and a first cancer-associated nucleic acid, said plurality of cells comprising at least one cancer cell and at least one non-cancer cell;

(ii) in at least one cancer cell removed from said plurality of cells, the absence or presence of at least one nucleic acid selected from the group consisting of a second cancer-specific nucleic acid and a second cancer-associated nucleic acid; and

(iii) in at least one non-cancer cell from the subject, the absence or presence of said nucleic acids from step (i) and step (ii),

wherein said first and second cancer-specific nucleic acids are different, and wherein said first and second cancer-associated nucleic acids are different; and

(b) determining, after administering the candidate anticancer therapy, a decreased presence of said nucleic acids in said cancer cell relative to the presence or absence of said nucleic acids in said non-cancer cell, and therefrom identifying an anticancer therapy.

39. (Amended) A method for identifying an anticancer agent, comprising:

(a) detecting in at least one cell, before and after contacting a candidate anticancer agent with a plurality of cells known to include or suspected of including a disseminated cancer cell or a micrometastasized cancer cell,

(i) an absence or presence of at least one nucleic acid selected from the group consisting of a first cancer-specific nucleic acid and a first cancer-associated nucleic acid, and

(ii) in at least one cancer cell removed from said plurality of cells, the absence or presence of at least one nucleic acid selected from the group consisting of a second cancer-specific nucleic acid and a second cancer-associated nucleic acid, and

(iii) in at least one non-cancer cell from said plurality of cells, the absence or presence of said nucleic acids from step (i) and step (ii),

wherein said first and second cancer-specific nucleic acids are different, and wherein said first and second cancer-associated nucleic acids are different; and

(b) determining, after contacting the candidate anticancer therapy with the cells, a decreased presence of any one or more of said nucleic acids in said cancer cell relative to the presence or absence of said nucleic acids in the non-cancer cell, and therefrom identifying an anticancer agent.

41. (Amended) A method for determining an increased risk for or presence of a disseminated cancer cell or a micrometastasizing cancer cell in a body fluid from a subject, comprising:

(a) dividing a plurality of cells into at least a first fraction and a second fraction, wherein each of the fractions comprises at least one cell and wherein the plurality of cells is from a body fluid of a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell, and wherein the first fraction has not been subjected to a method for isolating cancer cells from non-cancer cells, and wherein the second fraction comprises at least one cell that has been removed from said body fluid according to a method for isolating cancer cells from non-cancer cells;

(b) detecting in the first fraction an absence or presence of at least one first nucleic acid selected from the group consisting of a first cancer-specific nucleic acid and a first cancer-associated nucleic acid;

(c) detecting, in the second fraction, an absence or presence of at least one second nucleic acid selected from the group consisting of a second cancer-specific nucleic acid and a second cancer-associated nucleic acid; and

(d) detecting in at least one non-cancer cell from the subject an absence or presence of the at least one second nucleic acid that is detected in step (c),

wherein said first and second cancer-specific nucleic acids are different, wherein said first and second cancer-associated nucleic acids are different, wherein the presence of said first nucleic acid in the first fraction and an increased or decreased presence of the second nucleic acid in said second fraction relative to the presence or absence of said second nucleic acid in the non-cancer cell from the subject indicate an increased risk for having a disseminated cancer cell or a micrometastasized cancer cell.

42. (Amended) A method for determining an increased risk for or presence of a disseminated cancer cell or a micrometastasizing cancer cell in a body fluid from a subject, comprising:

(a) dividing a plurality of cells into at least a first fraction and a second fraction, wherein each of the fractions comprises at least one cell and wherein the plurality of cells is from a body fluid of a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell, and wherein the first fraction has not been subjected to a method for isolating cancer cells from non-cancer cells, and wherein the second fraction comprises at least one cell that has been removed from said body fluid according to a method for isolating cancer cells from non-cancer cells;

(b) detecting in the first fraction an absence or presence of at least one first cancer-specific nucleic acid;

(c) detecting in the second fraction an absence or presence of at least one second cancer-specific nucleic acid; and

(d) detecting in at least one non-cancer cell from the subject an absence or presence of the second cancer-specific nucleic acid that is detected in step (c),

wherein said first and second cancer-specific nucleic acids are different, wherein the presence of said first cancer-specific nucleic acid in said first fraction and an increased or decreased presence of said second cancer-specific nucleic acid in said second fraction relative to the presence or absence of said second cancer-specific nucleic acid in a non-cancer cell from the subject indicate an increased risk for having a disseminated cancer cell or a micrometastasized cancer cell.

43. (Amended) A method for determining an increased risk for or presence of a disseminated cancer cell or a micrometastasizing cancer cell in a body fluid from a subject, comprising:

(a) dividing a plurality of cells into at least a first fraction and a second fraction, wherein each of the fractions comprises at least one cell and wherein the plurality of cells is from a body fluid of a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell, and wherein the first fraction has not been subjected to a method for isolating cancer cells from non-cancer cells, and wherein the second fraction comprises at least one cell that has been removed from said body fluid according to a method for isolating cancer cells from non-cancer cells;

(b) detecting in the first fraction an absence or presence of at least one first cancer-specific nucleic acid;

(c) detecting in the second fraction an absence or presence of at least one second cancer-specific nucleic acid;

(d) detecting an absence or presence of at least one cancer-associated nucleic acid in at least one sample selected from the group consisting of (i) the first fraction and (ii) the second fraction; and

(e) detecting in at least one non-cancer cell from the subject an absence or presence of said second cancer-specific nucleic acid detected in step (c) and said cancer-associated nucleic acid detected in step (d),

wherein the presence of said first cancer-specific nucleic acid and of said cancer-associated nucleic acid in said first fraction and an increased or decreased presence of said second cancer-specific nucleic acid and of said cancer-associated nucleic acid in said second fraction relative to the presence or absence of said second cancer-specific nucleic acid and of said cancer-associated nucleic acid in a non-cancer cell from the subject indicate an increased risk for having a disseminated cancer cell or a micrometastasized cancer cell.

45. (Amended) The method of claim 41 wherein a nucleic acid selected from the group consisting of (i) a first cancer-associated nucleic acid and (ii) a second cancer-associated nucleic acid, said nucleic acid comprising a metastasis-associated gene, and wherein

the presence of said first cancer-associated nucleic acid comprising the metastasis-associated gene indicates an increased risk that a disseminated cancer cell has the ability to metastasize, and wherein an increased or decreased presence of said second cancer-associated nucleic acid comprising the metastasis-associated gene in said cancer cell relative to the presence or absence of said second cancer-associated nucleic acid comprising the metastasis-associated gene in a non-cancer cell from the subject indicates an increased risk that a disseminated cancer cell has the ability to metastasize.

46. (Amended) The method of either claim 45 or claim 60 wherein the metastasis-associated gene encodes a gene product selected from the group consisting of an angiogenesis factor, a motility factor, a growth factor, a matrix degradation factor and an adhesion factor.

49. (Amended) The method of either claim 45 or claim 60 wherein the nucleic acid is selected from the group consisting of DNA and RNA.

52. (Amended) The method according to any one of claims 41-42 wherein steps (a) - (d) are performed before and after administering a candidate anticancer therapy to a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell.

53. (Amended) The method according to claim 43 wherein steps (a) - (e) are performed before and after administering a candidate anticancer therapy to a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell.

Please add new claim 60 to read as follows:

60. (New) The method of claim 43 wherein the cancer-associated nucleic acid comprises a metastasis-associated gene, and wherein the presence of the cancer-associated nucleic acid comprising the metastasis-associated gene indicates an increased risk that a disseminated cancer cell has the ability to metastasize, and wherein an increased or decreased presence of the cancer-associated nucleic acid comprising the metastasis-associated gene in said cancer cell relative to the presence or absence of the cancer-associated nucleic acid comprising the metastasis-associated gene in a non-cancer cell from the subject indicates an increased risk that a disseminated cancer cell has the ability to metastasize.

REMARKS

Reconsideration of the present application in view of the present amendments and the following remarks is respectfully requested. Claims 21-22, 24-39, and 41-59 are currently pending. Claims 38-39 have been rejoined by the Examiner and have been examined on their merits. Applicants have amended claims 32, 38-39, 41-43, 45-46, 49, and 52-53 and have added new claim 60 to more clearly define the subject matter encompassed by Applicants' invention. Support for the amended claims and new claim may be found in the specification, for example, at page 4, lines 24-34, and at page 17, line 18 through page 19, line 1. No new subject matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to shows changes made.**" Also, for the Examiner's convenience an Appendix is attached following the "Version with markings," which contains all claims currently under examination in the present application pending entry of the present amendment.

PRIORITY

The Examiner notes that the present Application is a national stage application under 35 U.S.C. § 371 that has been converted from PCT application number PCT/EP98/05360, which has an international filing date of August 24, 1998 and claims priority to DE 197 36 691.0,